42

# Acute Liver Failure

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## DEFINITIONS

*Acute liver failure* (ALF) is defined as the onset of encephalopathy within 6 months after the occurrence of jaundice in a patient with hepatic injury but no prior history of liver disease. *ALF* replaces the older term for the same patient population, *fulminant hepatic failure*. Hepatic injury is usually defined as an international normalized ratio (INR) greater than 1.5 times normal with elevations of serum aminotransferases and total bilirubin. Other parameters further define hepatic failure based on the length of time from onset of jaundice to hepatic encephalopathy: *hyperacute hepatic failure* for periods shorter than 7 days, and *late-onset hepatic failure* for periods of 8 to 24 weeks.

## PATHOGENESIS

ALF develops as a result of severe, unrelenting hepatocyte necrosis. It is uncommon clinically but represents a medical emergency. ALF may result from infection with hepatitis viruses A, B, C, D, or E (see Chapter 41). Additionally, exposure to hepatotoxins such as acetaminophen, isoniazid, halothane, valproic acid, or mushroom toxins (e.g., those of *Amanita phalloides*) can produce ALF. Reye's syndrome, a disease that predominantly affects children, and acute fatty liver of pregnancy often resemble ALF; they are characterized by microvesicular fatty infiltration and little hepatocellular necrosis. Other rare causes of ALF include Wilson's disease, hepatic ischemia, autoimmune hepatitis, and malignancy (E-Figs. 42-1 and 42-2).

## CLINICAL PRESENTATION

The clinical presentation, by definition, includes jaundice and hepatic encephalopathy without clinical evidence of underlying chronic liver disease. Other common but nonspecific symptoms include nausea, vomiting, loss of appetite, right upper abdominal pain from hepatomegaly, fever, fatigue, dark urine, and clay-colored stools. Typically, the features of impaired hepatic synthetic and metabolic function predominate, with portal hypertension much less common than in patients with established cirrhosis.

## DIAGNOSIS

The clinical presentation of ALF can be dramatic, with jaundice and advanced systemic manifestations as the first indication of a severe and potentially threatening illness. A complete medical history is essential and should focus on potential exposure to viruses and hepatotoxins, pregnancy, an event associated with hypotension, and clues to suggest autoimmune causes.

Early laboratory testing should focus on assessing the severity of hepatic dysfunction and on detection of possible acetaminophen exposure, for which specific treatment must be initiated in a timely manner. Further specialized laboratory testing is designed to identify particular viral causes—with tests for anti–hepatitis A immunoglobulin M (IgM), hepatitis B surface antigen (HBsAg), anti–hepatitis B core antigen (anti-HBc) IgM, hepatitis D antigen, anti–hepatitis C antibody and/or hepatitis C virus RNA, anti–hepatitis E IgM, anti-varicella IgM, and herpes simplex IgM—or other causes (e.g., pregnancy test in females of childbearing age, ceruloplasmin level, autoimmune markers).

A negative serum acetaminophen level does not exclude acetaminophen overdose, because the drug is rapidly cleared in the blood. Importantly, acetaminophen overdose accounts for approximately 50% of all cases of ALF and 20% of all cases of presumed indeterminant causes in Western countries. Therefore, careful clinical assessment is essential to determine if an acetaminophen overdose may have occurred.

## TREATMENT

Treatment of ALF is largely supportive, because specific treatment for the underlying cause of liver failure is often not available. However, many processes that result in widespread liver cell necrosis and ALF are transient events, and liver cell regeneration with recovery of liver function often occurs if patients survive the initial insult. Acetaminophen toxicity and hypotension with hepatic necrosis are representative. In contrast, ALF resulting from viral hepatitis or idiosyncratic reactions to medications typically has a longer time course and an uncertain prognosis. In either case, meticulous supportive treatment in an intensive care unit setting has been shown to improve survival. Patients with ALF should be treated in centers with experience with this disease and with a liver transplantation program. Numerous complications can result from ALF, and each must be thoroughly identified and treated (Table 42-1). As liver failure progresses, a syndrome of multiorgan failure can result; this can include encephalopathy, coagulopathy, infection, and renal failure in the worst cases.

*Hepatic encephalopathy* is often the first and most dramatic sign of liver failure. The pathogenesis of hepatic encephalopathy in ALF remains unclear, and it differs from that associated with chronic liver disease or portal hypertension in two important aspects. First, it often responds to therapy only when liver function improves, and second, it is frequently associated with hypoglycemia or cerebral edema, two other potentially treatable causes of coma. Therapy for hepatic encephalopathy in ALF